

SPECIFICATION AMENDMENTS

Abstract (new). Coupled to the N-methyl-D-aspartate (NMDA) receptor complex is a strychnine-insensitive binding site for glycine. Pharmacological antagonism of glycine at this site may produce anticonvulsant activity. Twelve 4-urea-5,7-dichlorokynurenic acid derivatives were synthesized and subsequently screened in mice for anticonvulsant activity using MES, Met, and TTE tests, and a rotorod test was used to determine neurotoxicity. Seven of the derivatives had anticonvulsant activity in TTE testing at 100 mg/kg. One derivative had an ED₅₀ value of 134 mg/kg in TTE testing. Two derivatives had MES activity. Only one derivative was neurotoxic in the rotorod test. Compounds were screened at a 10 uM concentration for activity in displacing 5,7-dichlorokynurenic acid from synaptosomal membrane fragments. Nine of the twelve compounds synthesized and tested have demonstrated anticonvulsant activity. Thus, compounds of the present invention should be usable for the treatment of epilepsy, neurodegenerative diseases, and other syndromes involving inhibition or excessive stimulation of the NMDA receptor complex.